

EXHIBIT A

The following provides details for support for the amendments to Table 4 of the Specification and illustrates the amendments introduce no new matter.

In particular, the following provides sequence information as shown in originally filed Table 4 followed by the matching portion of preliminarily amended Table 4 (showing the proposed amendments).

Specification as Filed for SEQ ID NOS: 49 and 54:

Underlining in the original specification denotes support for amendments.

Re- gion	Epi- tope	Clone	Lib ^a	Framework 1	CDR 3	Framework 4	
VH	1	C15	1	QVFLQSGGAILVRPGASVLSCTTSQVTSFT	QITFDYDGGNYVAMK	WQQGTTVTASS	
		C9	1	-----	-----V-----	-----V-----	←SEQ ID NO: 49
		1B5	2	E--VE-----N--A-----			as originally filed
		C1	1	-----			
		S25	1	-----			
		1B6	2	--Q-----V---I---A---T-I			
		1C9	2	--Q-E-----V---I---G---			←SEQ ID NO: 54
		1D8	2	E-Q--E--PQ--K-SQ--LQ--T-TVT--I			as originally filed
		1G7	2	E-Q--E--PQ--K-SQ--LQ--T-TVT--I			

Specification as Amended for SEQ ID NOS: 49 and 54:

V _H Region		Sequence ^a				
Epitope 1		Framework 1	CDR 1	Framework 2	CDR 2	
		Framework 3	CDR3	Framework 4	Seq. ID No.	
C9	1	QVFLQSGGAILVRPGASVLSCTTSQVTSFT MATLTVDSSTAYMQLSFTSEDSAVYYCAR	SYMMN GITYVYDGGN- <u>YY</u> AMDY	WVKQSPQQGLSNIG WQQGTTVTVSS	NIMPSNSEIRPNKCFER 69	
1C9	2	QVqLkQSGAILVRPGsGVK1SC- <u>GGYtFi</u> KATLTvNeSSnTAYMeLor1TSEDSALYYCAR	DYAVH RgKq	WYFQshaksLEWIG WQQGTTVTVSS	v1st1yypdadyNphKqg 54	

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Specification as Filed for SEQ ID NO: 63:

Re- gion	Epi- tope	Clone	Lib ^a	Framework 1		CDR 1
		2	1A1	2	EVSLVSSGGGLVKGPGSIRLSGASGFTFS	DYVMS
			1F1	2	-----K-----A-----	S-G--
			C39	1	Q-Q-Q-----S-K-----A-----	---
			C23	1	Q-Q-Q-----K-----A-----	---Y
			2G5	2	-----K-----A-----	S-A--
			3C3	2	-----K-----A-----	S-A--
			3F4	2	-----K-----A-----	S-A--
			3H4	2	-----K-----A-----	S-A--

← SEQ ID NO: 63
as originally filed

Specification as Amended for SEQ ID NO: 63:

3P4	2	<u>E</u>	EVSLVSSGGGLVKGPGSIRLSGASGFTFS	STMS	WVRQIPHLRLDVA	TISDGGTETTYCDVKG
			RPTLSIRLAKHLVQLGSHLPSDDTMYTCAR	nlpydhr	Dy	WQQTETVTVSS
						63

Specification as Filed for SEQ ID NOS: 68 and 69:

Re- gion	Epi- tope	Clone	Lib ^a	Framework 1	CDR 1
	3	1R3	2	EVQLQSGGVVQPGSIRLSGASGFTFS	STVNR
	1C6	2	QI--LQ-----K-----A-----	---	
	2B6	2	VKLVNRPPLKPGSIRLSGASGFTFS	D-NNR	
	1G3	2	Q---Q---REL---A---VNR---K---Y---Y	---WTT	← SEQ ID NO: 68
	1H6	2	---Q---REL---A---VNR---K---Y---Y	---WTT	← SEQ ID NO: 69

as originally filed

Specification as Amended for SEQ ID NOS: 68 and 69:

1G5	2		EVQLQSGSGGVVQPGSIRLSGASGFTFS	STVNR	WVRQIPGSLDVA	diypgagstnynekkfs
			kaTILVQLSSTSTVQLSLGSLSDSAYTCAR	S	Elgd	anDy
						68
1H5	2		EVQLQSGSGGVVQPGSIRLSGASGFTFS	STVNR	WVRQIPGSLDVA	diypdgagstnynekkfs
			kaTILVQLSSTSTVQLSLGSLSDSAYTCAR	S	Elgd	anDy
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Specification as Filed for SEQ ID NOS: 72-80:

Clone	Lib	Framework 1	CDR 1	Framework 3	Framework 4	
C15	1	DIELTQSPAIMSASPGKRVIMTC	SASS	GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	PGSGTKLELR	SEQ ID NO: 72
C9	1	-----S-----I-----	---	---A-----SY-----	---A-----I---	SEQ ID NO: 73
1D5	2	-----A-----I-----	---S---	---V-----S-----A---	---G-----I---	SEQ ID NO: 74
C1	1	-----L-----I-----	---	---V-----A-----	---A-----	SEQ ID NO: 75
S25	1	-----L-----I-----	---V---S---	---V-----S-----A---	---A-----I---	SEQ ID NO: 76
1B6	2	-----SLAV-L-QRA-IG-	PA-SYV	---I-----E-DFT--INPY--D-V---	---A-----	SEQ ID NO: 77
1C9	2	-----SLAV-L-QRA-IG-	PA-SYV	---I-----R-DFT--INPY--D-V---	---A-----I---	SEQ ID NO: 78
1B8	2	-----L-----I-----	---	---A-----S-----A---	---A-----	SEQ ID NO: 79
1G7	2	-----L-----I-----	---	---A-----S-----A---	---A-----	SEQ ID NO: 80

as originally filed

Specification as Amended for SEQ ID NOS: 72-80:

V ^H Region Epitope 1						
Clone	Lib	Framework 1	CDR 1	Framework 2	CDR 2	
		Framework 3	CDR 3	Framework 4	No	Seq ID
C15	1	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	72
C9	1	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	73
1D5	2	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	74
C1	1	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	75
S25	1	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	76
1B6	2	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	77
1C9	2	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	78
1E8	2	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	79
1G7	2	DIELTQSPAIMSASPGKRVIMTC G ¹ GVPIRFSGSGSSTSYSLTISRMEAEASATYYC	SASS SVSNMY	WYQQKPGSSPRLLIY	DTSNLAS	80

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Specification as Filed for SEQ ID NOS: 81-88:

Clone	Lib ^a	Framework 1	CDR 1	CDR 3	Framework 4	
1A1	2	DIELTQSPASLAVSLGQRATISC	RASESVDSYGNFPMH	QWQKPGQPKLLIY	FGSGTKLEAKR	SEQ ID NO: 81
1F1	2	-----T-----	-----	-----	-----	SEQ ID NO: 82
C39	1	-----R-----	-----	-----	-----	SEQ ID NO: 83
C25	1	-----H--Q	-----P	-----	-----	SEQ ID NO: 84
2G5	2	-----DMSA-P-RKVITP	S--S	SV-Y--	SSSY--	SEQ ID NO: 85
3C3	2	-----DMSA-P-EKVITP	-----H--Q	SSSY--	-----	SEQ ID NO: 86
3F4	2	-T-----DMSA-P-EKVITP	S--S	SV-Y-Y	SSSY-D-	SEQ ID NO: 87
3H4	2	-----DMSA-P-EKVITP	---S-	VSS-YL-	SSSY-P-	SEQ ID NO: 88 as originally filed

Specification as Amended for SEQ ID NOS: 81-88:

1A1	2	DIELTQSPASLAVSLGQRATISC GVPARFSGSGSKITLTIDPVEADDAATYYC	RASESVDSYGNFPMH QWQKPGQPKLLIY	WYQKPGQPKLLIY FGSGTKLEAKR	LASNLES	81
1F1	2	DIELTQSPETSLAVSLGQRATISC GVPARFSGSGSKITDFTLIDPVEADDAATYYC	RASESVDSYGNFPMH QWQKPGQPKLLIY	WYQKPGQPKLLIY FGSGTKLEAKR	LASNLES	82
C39	1	DIELTQSPASLAVSLGQRATISC GVPARFSGSGSKITDFTLIDPVEADDAATYYC	RASESVDSYGNFPMH QWQKPGQPKLLIY	WYQKPGQPKLLIY FGSGTKLEAKR	LASNLES	83
C25	1	DIELTQSPASLAVSLGQRATISC GVPARFSGSGSKITDFTLIDPVEADDAATYYC	RASESVDSYGNFPMH QWQKPGQPKLLIY	WYQKPGQPKLLIY FGSGTKLEAKR	LASNLES	84
2G5	2	DIELTQSPAIMASpGekvtctc GVPARFSGSGSKITLTIDPVEADDAATYYC	RASESVDSYGNFPMH QWQKPGQPKLLIY	WYQKPGQPKLLIY FGSGTKLEAKR	LASNLES	85
3C3	2	DIELTQSPAIMASpGekvtctc GVPARFSGSGSKITLTIDPVEADDAATYYC	RASESVDSYGNFPMH QWQKPGQPKLLIY	WYQKPGQPKLLIY FGSGTKLEAKR	LASNLES	86
3F4	2	DIELTQSPAIMASpGekvtctc GVPARFSGSGSKITLTIDPVEADDAATYYC	RASESVDSYGNFPMH QWQKPGQPKLLIY	WYQKPGQPKLLIY FGSGTKLEAKR	LASNLES	87
3H4	2	DIELTQSPAIMASpGekvtctc GVPARFSGSGSKITLTIDPVEADDAATYYC	RASESVDSYGNFPMH QWQKPGQPKLLIY	WYQKPGQPKLLIY FGSGTKLEAKR	LASNLES	88

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Specification as Filed for SEQ ID NOS: 94 and 95:

Clone	Sequence ^b	
	CDR 2	Framework 3
1F3	SASNLAS	GVPSEFSGSGGTSYSLTISVEAEDAATYYC
2E8	ET-----	---A---GAG---Y-----

← SEQ ID NO: 94
 ← SEQ ID NO: 95
 as originally filed

Specification as Amended for SEQ ID NOS: 94 and 95:

<u>SL</u>			
1F3	2	DIETQSPASMGASPGKVNTTC GVPSRFSGGGSGTSYSLTISVEAEDAATYYC	RATSS VSSSYLH QQTIGTPTT FGGSKLEIKR
2E8	2	DIETQSPtMaASPGKLiTiTC GVPSRFSGGGSGTSYSLTIGMRAEDVATYYC	sAsSS iGsnYLH WYQQRpGfSPKLIIV FGGSKLEIKR
			SASNLAS 94 SASNLAS 95

M

EXHIBIT B

The following illustrates that the amendments to the claims to correct the sequence identifiers do not introduce new matter.

The relevant parts of Table 11 on page 85-88, paragraph [0241] of the Specification **as originally filed** are reproduced below.

[0241] Table 11 amino acid sequences for affinity matured and/or modified antibodies.

Heavy Chains				
Clone	Framework 1	CDR1	Framework 2	CDR2
huC25	QVQLQESGGGLVOPGGSLRLSC AASGFTFS (SEQ ID	DYYMY (SEQ ID NO:87)	WVRQAPGKGLEW VA (SEQ ID	TISDGGSYTYYPD SVKG (SEQ ID
	NO:86)		NO:88)	NO:89)
...				
Heavy Chains cont'd				
	Framework 3	CDR3	Framework 4	
huC25	RFTISRDN SKNTLYLQMNSLRA EDTAMYVCSR (SEQ ID NO:126)	YRYDDAMDY (S EQ ID NO:127)	WGQGT LVT VSS (S EQ ID NO:128)	
...				
Light Chains				
Clone	Framework 1	CDR1	Framework 2	CDR2
huC25	EIVLTQSPATLSLSPGERATIS	RASESVDSYGH	WYQQKPGQAFRL	RASNLEP (SEQ
	C (SEQ ID NO:156)	SFMQ (SEQ ID NO:157)	LIY (SEQ ID NO:158)	ID NO:159)
...				
Light Chains cont'd.				
Clone	Framework 3	CDR3	Framework 4	
huC25	GIPARFSGSGSGTDFTLTISSL RPEDFAVYYC (SEQ ID NO:196)	QQSNEDPFT (S EQ ID NO:197)	FGQGT KVEIKR (S EQ ID NO:198)	

EXHIBIT B

The relevant parts of Table 11 as amended pursuant to the **Preliminary Amendment** filed April 19, 2004 are reproduced below.

At pages 85-88, amend Table 11 as follows:

[0241] Table 11 amino acid sequences for affinity matured and/or modified antibodies.

Heavy Chains				
Clone	Framework 1	CDR1	Framework 2	CDR2
huC25	QVQLQESGGGLVQPGGSLRLSC AASGFTFS (SEQ ID NO: 86138)	DYYMY (SEQ ID NO: 87139)	WVRQAPGKGLEW VA (SEQ ID NO: 88140)	TISDGGSYTYYPD SVKG (SEQ ID NO: 89141)

...

Heavy Chains cont'd				
	Framework 3	CDR3	Framework 4	
huC25	RFTISRDN SKNTLYLQMNSLRA EDTAMYYCSR (SEQ ID NO: 126178)	YRYDDAMDY (S EQ ID NO: 127179)	WGQGLTVTVSS (SEQ ID NO: 128180)	

...

Light Chains				
Clone	Framework 1	CDR1	Framework 2	CDR2
huC25	EIVLTQSPATLSLSPGERATIS C (SEQ ID NO: 156208)	RASESVDSYGH SFMQ (SEQ ID NO: 157209)	WYQQKPGQAPRL LIY (SEQ ID NO: 158210)	RASNLEP (SEQ ID NO: 159211)

...

Light Chains cont'd.				
Clone	Framework 3	CDR3	Framework 4	
huC25	GIPARFSGSGGTDFTLTISSL EPEDFAVYYC (SEQ ID NO: 196248)	QOSNEDPFT (SEQ ID NO: 197249)	FGQGTVEIKR (SEQ ID NO: 198250)	

EXHIBIT B

The sequence information of SEQ ID NOS: 139, 141, 179, 209, 211, and 249, as shown in the enclosed Sequence Listing, as well as their one letter code sequences are as follows.

As shown in the Sequence Listing:

One-Letter Code:

Sequence in the Specification as Amended in the Preliminary Amendment:

<210> 139
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> single chain antibody fragment

<400> 139
 Asp Tyr Tyr Met Tyr
 1 5

SEQ ID NO: 139
 DYYMY

DYYMY (SEQ
 ID
 NO: ~~87139~~)

<210> 141
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> single chain antibody fragment

<400> 141
 Thr Ile Ser Asp Gly Gly Ser Tyr Thr Tyr Tyr
 Pro Asp Ser Val Lys
 1 5 10 15
 Gly

SEQ ID NO: 141
 TISDGGSYTYYPDSVKG

TISDGGSYTYYPD
 SVKG (SEQ ID
 NO: ~~89141~~)

<210> 179
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> single chain antibody fragment

<400> 179
 Tyr Arg Tyr Asp Asp Ala Met Asp Tyr
 1 5

SEQ ID NO: 179
 YRYDDAMDY

YRYDDAMDY (S
 EQ ID
 NO: ~~127179~~)

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<210> 209
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain antibody fragment

<400> 209
Arg Ala Ser Glu Ser Val Asp Ser Tyr Gly His
Ser Phe Met Gln
1 5 10 15

SEQ ID NO: 209
RASEVDSYGHSEFMQ

RASEVDSYGH
SEFMQ (SEQ ID
NO: ~~457~~209)

<210> 211
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain antibody fragment

<400> 211
Arg Ala Ser Asn Leu Glu Pro
1 5

SEQ ID NO: 211
RASNLEP

RASNLEP (SEQ
ID NO: ~~459~~211)

<210> 249
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> single chain antibody fragment

<400> 249
Gln Gln Ser Asn Glu Asp Pro Phe Thr
1 5

SEQ ID NO: 249
QQSNEDPFT

QQSNEDPFT
(SEQ ID
NO: ~~497~~249)